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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/857,557	06/04/2001	Rebecca Cahoon	BB-1297	5031

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EXAMINER	
GEBREYESUS, KAGNEW H	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 08/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/857,557	CAHOON ET AL.	
	Examiner	Art Unit	
	Kagnew H Gebreyesus	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-37* is/are pending in the application.

4a) Of the above claim(s) *11-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *25-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants election without traverse of Group 1, corresponding to claims 25-37 is acknowledged. Claims 1-24 have been cancelled. Claims 25-37 are under consideration.

Priority

Priority for benefit of US Provisional application No. 60/110,865 is acknowledged as it pertains to the subject matter of the group and species elected.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 25-27, 30-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Does the complement of the nucleotide sequence also include the genus of polynucleotides complementary to SEQ ID NO: 7? It is suggested to amend the claims to read as: a full-length complement of the nucleotide sequence of (a)" for example.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 25-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of complementary nucleic acid sequences. The specification teaches the structure of the polynucleotide sequence of SEQ ID NO: 7 and full length complementary sequence by virtue of the double stranded nature of DNA. However no disclosure of specific fragments of the complementary strand have been disclosed. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 25-27, 30-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide of SEQ ID NO: 7 encoding a polypeptide of SEQ ID NO: 8 having 1-deoxy-D-xylulose 5-phosphate reductoisomerase activity, does not reasonably provide enablement for a polynucleotide/polypeptide with only 93% -98% identity to an enzyme of SEQ ID NO: 8 (claims 25) based on the CLUSTAL V method and having 1-deoxy-D-xylulose 5-phosphate reductoisomerase activity. In addition the specification while being enabling for a full length complementary sequence to SEQ ID NO: 7 does not enable any fragment complementary to any portion of the polynucleotide/polypeptide sequence of SEQ ID NO: 7/SEQ ID NO: 8. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 25-27, 30-37 are so broad as to encompass any polynucleotide encoding a polypeptide having 1-deoxy-D-xylulose 5-phosphate reductoisomerase activity with 93%-95% identity to an enzyme of SEQ ID NO: 8 based on the CLUSTAL V method. The claims also encompass any fragment complementary to the polynucleotide/polypeptide of SEQ ID NO: 7/SEQ ID NO: 8. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims. Since the polynucleotides encoding the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a nucleic acid sequence encoding the polypeptide's amino acid sequence and obtain the desired activity in this case 1-deoxy-D-xylulose 5-phosphate reductoisomerase activity requires a knowledge of and guidance with regard to which nucleotide residues or encoded amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. In addition a nucleic acid sequence comprising SEQ ID NO: 8 encompasses an enormous number and diversity of sequences beyond the scope enabled by the instant specification. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of SEQ ID NO: 7/SEQ ID NO: 8 having 1-deoxy-D-xylulose 5-phosphate reductoisomerase activity.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims (93-95% sequence identity), and the positions within a polynucleotide/polypeptide's sequence where nucleic acid/amino acid modifications can be made with a reasonable expectation of

success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications of any polynucleotide encoding a polypeptide with 93%-95% identity to SEQ ID NO: 8 based on the CLUSTAL V method and having 1-deoxy-D-xylulose 5-phosphate reductoisomerase activity or all complementary fragments because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting enzyme name activity; (B) the general tolerance of the polynucleotide encoding the polypeptide with 1-deoxy-D-xylulose 5-phosphate reductoisomerase activity to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues in the polynucleotide sequence (SEQ ID NO: 7) residues encoding the polypeptide with an expectation of obtaining the desired biological function, i.e. 1-deoxy-D-xylulose 5-phosphate reductoisomerase activity; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any polynucleotide/ polypeptide with only 93% -98% identity to an enzyme of SEQ ID NO: 8 (claims 25) and having 1-deoxy-D-xylulose 5-phosphate reductoisomerase activity with an enormous number of possible nucleotide/amino acid modifications of the polynucleotide/polypeptide of SEQ ID NOS: 7/SEQ ID NO: 8. In addition

the specification while being enabling for a full-length complementary sequence to SEQ ID NO: 7 does not enable for any complementary fragment at any portion of the polynucleotide/polypeptide sequence of SEQ ID NO: 7/SEQ ID NO: 8.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of a polynucleotide sequence encoding a polypeptide having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 32 and 33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using the vector comprising the polynucleotide of SEQ ID NO: 7 to transform an isolated cell or an isolated plant cell in a method of producing a transgenic plant or a seed comprising the recombinant vector, does not reasonably provide enablement for transforming any cell or organism including a cell within an animal or human with said recombinant vector. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized ln re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988). The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or

unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claims encompass transforming any cell of a microorganism or any cell within any multi-cellular organism including animals and humans. The specification provides guidance and examples for making a recombinant vector comprising the polynucleotide sequence of SEQ ID NO: 8 and the use of said recombinant vector to transform an isolated plant cell and a method of producing a transgenic plant and a seed comprising the polynucleotide sequence of SEQ ID NO: 8. However, the specification does not teach an organism such as an animal or human comprising a cell transformed with said recombinant vector or a

method making any transgenic organism such as an animal or human.

The standard for meeting the enablement requirement is whether one of skill in the art can make the invention without undue experimentation. The amount of experimentation to make the claimed invention is enormous and undue. Such experimentation entails constructing vectors suitable for any organism, method of transforming any organism and determining that the organism is a transgenic organism. Thus, performing such task is well outside the realm of routine experimentation and specification regarding the specific cell or organism to be transformedor the method of positive selection of an organism transformed with said recombinant vector.

The Examiner finds that one skilled in the art would require additional guidance, such as information specific to the isolated cell or the organism from which the cell is derived or the method for transforming any cell or the transgenic organism claimed. Without such a guidance, the experimentation left to those skilled in the art is undue.

The recitation "a cell comprising the recombinant DNA construct" encompasses any organism including animals and humans. It is suggested that applicants amend claim 32 to read as: " a method for transforming an isolated cell or an isolated plant cell" and

Claim 33 to read as: "an isolated cell or an isolated plant cell" (in claim 33) to overcome this rejection.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

4. Claims 25-27, 30-36 are rejected under 35 U.S.C. 102(a) as being anticipated by Takahashi et al. (Proc. Natl. Acad. Sci. Vol. 95, pp, 9879-9884, August 1998 complete DNA and protein sequence disclosed by GenBank accession No. AB013300). Takahashi et al. disclose a polynucleotide sequence encoding 1-deoxy-D-xylulose 5-phosphate reductoisomerase from several bacteria. Although the complementary sequence of these polynucleotides do not show a high level of identity to the full length complementary sequence of 1-deoxy-D-xylulose 5-phosphate reductoisomerase of the present invention, short complementary sequences of these sequences anticipate embodiments in claims 25-27, 30-36.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kagnew H Gebreyesus whose telephone number is 571-272-2937. The examiner can normally be reached on 8:30am-5: 30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Achutamurthy ponnathapura can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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